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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/789,303	CLARK ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *15-17, 20,* is/are withdrawn from consideration.

5)☒ Claim(s) *18* is/are allowed.

6)☐ Claim(s) *1-3,9-14,19 and 21-30* is/are rejected.

7)☒ Claim(s) *4-8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5-0-01

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-14, 18-19, and 21-30 (in part) in the reply filed on 5/6/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 15-17, 20, and 21-29 (in part) are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/6/2005.

Claim Objections

Claims 21-29 are objected to for depending from a non-elected claim (claim 20). The claims all depend, in the alternative, from the non-elected method of claim 20.

Claim 6 and 7 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 recites a rAd "derived from" simian Ad SV-20. It cannot be determined how close to the original or wild-type SV-20 the derivative rAd might be. Therefore, the metes and bounds of the claimed subject matter are unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 14, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel biological materials, specifically the simian adenovirus strain deposited as ATCC No. VR-199. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, a deposit of the biological materials may satisfy the requirements of 35 U.S.C. § 112. The specification does not disclose a repeatable process to obtain the biological material and it is not apparent if the biological materials are readily available to the public. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a

statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon an issuance of patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may provide an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. §§ 1.807); and

(e) the deposit will be replaced if it should ever become unviable.

Applicant's attention is directed to M.P.E.P. § 2400 in general, and specifically to §2411.05, as well as 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however,

Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information. Finally, Applicant is advised that the address for the ATCC has recently changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection

10801 University Boulevard

Manassas, VA 20110-2209

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 10-13, 21, 23, 24, and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Natsoulis et al (U.S. Patent 6,027,931, 2000). The claims recite a rAAV-producing cell comprising a rAAV genome, AAV rep-cap proteins and AAV helper functions wherein said cell expresses Rep 78/68 at about wild-type levels and overexpresses Rep 52/40 proteins. Also claimed is a method of producing rAAV by culturing the above cell. Also claimed is a method for generating a rAAV-producing cell by providing AAV helper functions to a cell comprising a rAAV genome and rep-cap proteins followed by introducing an expression cassette encoding Rep 52/40 proteins. The Rep 52/40 proteins may be supplemental, and the supplemental Rep 52/40 may introduced by an additional expression cassette. The AAV helper

functions may be provided by a helper virus. The cell may be 293, low passage 293 cells, or any of those listed in claim 30.

Natsoulis et al disclose a the transfection of 293 cells (obtained from the ATCC, column 15, lines 18-19, and thus considered low-passage) with an AAV vector (pVlacZ), a helper virus (pladeno5) and various helper constructs encoding rep-cap (column 15, Example 1). The AAV vector may include rep-cap coding sequences and must contain the AAV ITRs (column 6, last6 paragraph), and thus is a rAAV genome by applicants' definition (page 5, second full paragraph). The adenovirus (pladeno5) provides "AAV helper functions" as described by applicants on page 2 and the various constructs shown in Fig. 1 provide rep-cap proteins. In the instance of pRCM.globinpolyA, Rep 78/68 is about that of wild-type/p5 expression, and Rep 52/40 is overexpressed. See column 15, last paragraph, Fig. 2, and column 12, second paragraph. For clarity, Natsoulis defines Rep78/68 as the "long forms" of Rep protein and Rep 52/40 as the "short forms" (see column 6, lines 21-30). The 293 cells of Example 1 were cultured and infectious AAV-LacZ was produced, see column 16, Example 2. The AAV vector and AAV helper function (i.e. the Rep/Cap constructs of Fig. 1) may be transfected into the cell sequentially (column 12, lines 39-42). The Rep 52/40 provided by the AAV helper constructs are considered "supplemental" to any encoded by the AAV vector.

Claims 1-2, 10-13, 21, 23, 24, and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Xiao et al (J. Virol., 1998). The claims are described above.

Xiao et al disclose transfection of 293 cells with a rAAV genome (pdx31-AAV) and rep-cap proteins from several vectors (Fig. 1A). Rep78/68 expression was attenuated (considered,

absent a precise definition, to be "about" the wild-type level of expression) and Rep 52/40 expression increased upon introduction of an extra copy of the p5 promoter. See page 2226, first column, last paragraph, pXX2 diagram of Fig. 1A, and Table 1. pXX2 is considered to introduce supplemental Rep52/40 to that of the AAV vector plasmid. Adenovirus was used as a helper virus (see legend of Table 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22, 26, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) in view of Hardy (U.S. Patent 6,429,001, 2002, effective filing date of 1/26/2000).

The claims are described above except the cell may be HeLa, Vero, MRC-5, or WI-38.

The teachings of Natsoulis et al are described above and applied as before. Natsoulis teaches the specific use of 293 cells, but also that the host cell may be any mammalian cell that can be used as recipients of AAV plasmids or vectors (column 8, lines 37-58).

Hardy teaches that AAV has a broad host range and that with transfection techniques to deliver rAAV genomes, a broad array of host cells could be used to produce rAAV. Specific cell types listed are HeLa, WI-38, MRC-5, and Vero. Hardy further teaches that generally, any cell-line that is easily cultured, endogenous virus-free and helper virus permissive is a suitable host cell. See column 9, first paragraph.

The claimed methods and cells are disclosed by Natsoulis et al with the exception of the specific cell types. The ordinary skilled artisan, seeking an efficient method to produce rAAV, would have been motivated to use specific cell lines of Hardy because Hardy teaches them to be well known types of cell lines that have utility for producing rAAV. It would have been obvious for the skilled artisan to do this because of the known benefit of efficiently generating high-titer, pure stocks of rAAV for laboratory use or for gene transfer (i.e. gene therapy) trials. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) in view of Murphy (U.S. Patent 6,635,476, 2003, effective filing date of 10/15/1999).

The claim is described above, except the cell may be PerC.6.

The teachings of Natsoulis et al are described above and applied as before.

Murphy teaches the usefulness of the PERC.6 cell line in conjunction with E1-deleted adenoviruses and adeno-associated viruses.

The claimed method and cell are disclosed by Natsoulis et al with the exception of the PerC.6 cell type. The ordinary skilled artisan, seeking an efficient method to produce rAAV, would have been motivated to use PerC.6 cell line of Murphy because Murphy teaches it to be a well known type of cell line that has utility for producing rAAV and adenoviruses. It would have been obvious for the skilled artisan to do this because of the known benefit of efficiently generating high-titer, pure stocks of rAAV for laboratory use or for gene transfer (i.e. gene therapy) trials. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al and Hardy as applied to claims 22, 26, 28, and 29 above, and further in view of Potash et al (U.S. Patent 5,911,998, 1999).

The claims are described above except the cell may be MRC-5, WI-38, or FRhL-2.

The teachings of Natsoulis et al and Hardy are described above and applied as before.

Potash et al teach the use of the MRC-5, WI-38, or FRhL-2 cell lines in the preparation of a viral vaccines. This is due to the FDA approval of these cell lines as sources for vaccine production. See column 2, third full paragraph.

The claimed methods and cells are disclosed by Natsoulis et al with the exception of the MRC-5, WI-38, or FRhL-2 cell types. Hardy teaches the use of these cell lines, except for FRhL-2, and that in general most mammalian cell lines are useful for rAAV production. The ordinary skilled artisan, seeking an efficient method to produce rAAV, would have been motivated to use the MRC-5, WI-38, or FRhL-2 cell lines of Hardy and Potash et al because Hardy teaches MRC-5 and WI-38 to be well known types of cell lines that have utility for producing rAAV and Potash et al teach the MRC-5, WI-38, and FRhL-2 cell lines as useful in viral vaccine preparation. It would have been obvious for the skilled artisan to do this because of the known benefit of efficiently generating high-titer, pure stocks of rAAV for laboratory use or for gene transfer (i.e. gene therapy) trials. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

Claim 4-5 and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 18 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1633

CELIAN QIAN
PATENT EXAMINER